

EE

Appendix E

Krieg '646 Patent Claims Corresponding to Proposed Count 2

Applicants identify claims 3, 11, 12, 17, 21, 25, 27, 37 and 38 of the Krieg '646 patent as corresponding to the proposed count 2. Krieg '646 patent Claim 3 is the first alternative of proposed count 2. All of the dependent claims (11, 12, 17, 21, 25, 27, 37 and 38) are directed to compositions containing an allergen. As a preliminary matter, claims 11, 17, 21, 25 and 37 recite Markush groups which recite, inter alia, "allergen" as a species of antigen, and to the extent "allergen" is contained in the Markush group these claims correspond to proposed count 2, as discussed more fully below.

Dependent claim 11 is directed to a composition comprising a plasmid containing a immunostimulatory CG-containing polynucleotide sequence and an antigen, wherein the antigen is an allergen (a species of the recited Markush group). Dependent claim 12 is also directed to this plasmid composition with allergen. Dependent claim 17 is directed to a composition comprising a CG-containing immunostimulatory nucleic acid of 8 to 100 nucleotides in length and an antigen, wherein the antigen is an allergen (a species of the recited Markush group). Dependent claim 21 is directed to a composition comprising a CG-containing immunostimulatory nucleic acid of at least 8 nucleotides in length and an antigen, wherein the antigen is an allergen (a species of the recited Markush group). Dependent claim 25 is directed to a composition comprising a CG-containing immunostimulatory nucleic acid of 8 to 40 nucleotides in length and an antigen, wherein the antigen is an allergen (a species of the recited Markush group). Dependent claim 37 is directed to a composition comprising a CG-containing immunostimulatory nucleic acid of at least 8 nucleotides in length (wherein at least one nucleotide has a phosphate backbone modification) and an antigen, wherein the antigen is an allergen (a species of the recited Markush group). Dependent claim 38 recites that the antigen is an allergen.

With respect to all of the above composition claims, an allergen-containing composition is obvious in view of a method to treat an allergy using a CG-containing immunostimulatory sequence and an antigen which causes an allergic response, or allergen. One must use such a composition in practicing the method of proposed count 2. As discussed above, oligomeric forms of CG-containing immunostimulatory polynucleotides are obvious in view of a functionally corresponding plasmid (*i.e.*, a plasmid containing the same functional sequence). With respect to claim 21, a plasmid anticipates a polynucleotide of at least 8 nucleotides in length.

“Allergen” is a patentably distinct species with respect to the genus “antigen”. As discussed above, an allergen is a type of antigen which elicits an unwanted, inappropriate immune response which is accompanied by production of allergy-associated IgE antibodies. Without the understanding that CG-containing immunostimulatory polynucleotides effect a Th1 shift, and thus reduce IgE production, one skilled in the art would not consider it obvious to combine an allergen with these immunostimulatory polynucleotides. The Krieg '646 patent specification reflects this reasoning. As discussed above, the Krieg '646 patent specification states that, based on the ability of the claimed immunostimulatory CG-containing polynucleotides to effect a Th1 shift (*i.e.*, shifting the immune response from a Th2 response toward a Th1 response), the immunostimulatory polynucleotides could be used to treat or prevent an allergy. Col. 34, lines 18-26. Neither of Krieg's earlier patent applications (to which priority is claimed) contain any disclosure of the Th1 shift or of using allergens in conjunction with CG-containing immunostimulatory polynucleotides. Instead, these earlier-filed cases only generally describe using antigen, without ever referring to using allergens. Nor do either of Krieg's earlier-filed cases make any reference to using CG-containing immunostimulatory polynucleotides in the allergy context. Thus, in terms of compositions, an allergen-based composition is a non-obvious species with respect to an antigen-based composition.

Dependent claim 27 is directed to a method of inducing an antigen-specific immune response comprising administering a vaccine including an antigen and an immunostimulatory

nucleic acid sequence of any of claims 6, 14, 18 or 22, wherein the antigen is an allergen (a species of the recited Markush group). Eliciting an antigen-specific immune response by combining the claimed immunostimulatory nucleic acid sequence(s) with an allergen is obvious in view of the proposed count, in which an allergen (*i.e.*, antigen which stimulates allergy-associated IgE production) combined with immunostimulatory sequence is administered to a subject.

Applicants submit that the above claims do not define separate patentable inventions within the meaning of 37 C.F.R. § 1.601(n).